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10/826,563	04/16/2004	Mark A. Hoffman	CRNI.114071	2108

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EXAMINER	
SIMS, JASON M	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,563	HOFFMAN ET AL.	
	Examiner	Art Unit	
	JASON M. SIMS	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-8,10,12-15,17 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5-8, 10, 12-15, 17 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 6/21/2010, have been fully considered. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicants have amended their claims, filed 6/21/2010, and therefore rejections newly made in the instant office action have been necessitated by amendment.

Claims 1, 3, 5-8, 10, 12-15, 17, and 19-23 are the current claims hereby under examination.

Claim Rejections - 35 USC § 112

Response to Arguments

Applicant's arguments, filed 6/21/2010, with respect to the rejection of claims under 35 USC 112 First paragraph have been fully considered and are persuasive because of applicant's arguments. Therefore the rejection has been withdrawn.

The following rejection has been modified, which was necessitated by amendment:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5-8, 10, 12-15, 17 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over ICHIKAWA (Internal Medicine (July, 2000) vol. 39, no. 7, pp. 523-524) (This reference has been submitted via IDS filed on 4/11/2008 and therefore will not be cited on a separate 892 form) in view REINHOFF et al. (US 2002/0049772 A1, filed 5/26/2000), in view of Fey et al. (US A/N 2002/0038227), and further in view of Fiedotin et al. (US P/N 7,509,263) and further in view of Hogan (US P/N 2002/0110823 with a priority date of 7/11/2000).

The claims are drawn to a computer system, computer readable medium and a method in a computer system for generating an output including information regarding the likelihood a person has a gene variant indicative of an atypical event, comprising the steps of:

a) displaying a first user interface to a clinician, the user interface configured to display and receive clinical agent information including at least one identifier of a clinical agent;

b) receiving from the user interface the clinician's inputs including at least one identifier of a clinical agent and a dosage of the clinical agent, wherein receiving includes receiving a selection of an entry in a listing of clinical agents on the first user interface and a selection of the dosage from a range of dosages recommended for the clinical agent associated with the selected entry;

c) accessing a data structure to determine if a gene variant is known to be associated with one or more atypical events for the identifier of the clinical agent received from the clinician, wherein the data structure includes an agent-gene association table;

d) inquiring if the person to whom the clinical agent is to be administered has a stored genetic test result value for the gene variant, wherein inquiring includes accessing an electronic medical record (EMR) of the person;

e) accessing hereditary information for the person if the person does not have a genetic test result value for the genetic variant, the hereditary information being information that may be utilized to determine if the person has a predisposition for certain conditions, wherein the hereditary information is obtained from the EMR of the person;

f) utilizing the hereditary information for the person to determine the likelihood the person has the gene variant; and

g) generating an output including information regarding the likelihood a person has a gene variant indicative of an atypical event based on hereditary information; and

h) displaying a second user interface to the clinician, the user interface configured to display the output regarding the likelihood the person has the gene variant indicative of an atypical event for the identifier of the clinical agent received from the clinician.

With regards to limitations of claims 1, 8 and 15: ICHIKAWA teaches at page 523, first column, 2nd and 3rd paragraphs data related to azathioprine or mercaptopurine (clinical agents), which reads on a limitation of step b) of clinical agent information, the clinical agent information including an identifier of the agent. ICHIKAWA at page 523, 3rd and 4th paragraphs, teaches about thiopurine S-methyl transferase (TPMT), which has genetic polymorphisms associated with one or more atypical events for the clinical agents, which reads on limitations of step c) accessing a data structure to determine if a gene variant is known to be associated with one or more atypical events for the clinical agent information. ICHIKAWA at page 523, first column, last 5 lines, teaches it is quite important to know in advance whether a patient who will be treated with thiopurine derivitives, has genetic polymorphism at TPMT sites, which reads on limitations of step d) inquiring if the person has a stored genetic test result value for the gene variant. ICHIKAWA at page 523, second column, first paragraph teaches a method for processing hereditary (genetic) information related to response to azathioprine or mercaptopurine (clinical agents) wherein genetic tests results for individual patients are accessed, which reads on limitations of step e) accessing hereditary information for the person if the person does not have a genetic test result value for the genetic variant. ICHIKAWA further teaches at page 523, first column, last paragraph and second column first paragraph that the presence of a polymorphism is then determined, wherein particular mutations or polymorphisms are associated with atypical clinical events (side effects) of administration of various drugs, and a decision made to change a drug dosage, which reads on step f) utilizing the hereditary information for the person to

determine the likelihood the person has the gene variant. Since drug dosages are based on the genetic testing results in the method of ICHIKAWA, the method necessarily includes a step of outputting the test results, which reads on step g) generating an output including information regarding the likelihood a person has a gene variant indicative of an atypical event based on hereditary information.

ICHIKAWA does not explicitly teach the computer aspect of accessing a data structure as in a limitation of step b), or the computer implemented aspects of the instant steps.

Rienhoff et al. at the abstract, teach a computer program product that allows identification of a susceptibility locus in individuals using genetic screening methods to assess their risk of certain diseases wherein the information can be used to gauge drug responses.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the computer implemented methods for allowing identification of a susceptibility locus in individuals using genetic screening methods to assess their risk of certain diseases wherein the information can be used to gauge drug responses as taught by Rienhoff et al. to identify individuals with genetic polymorphisms of TPMT sites prior to the administration of the clinical agents. This is because ICHIKAWA at page 524, states that it would be possible to anticipate the effectiveness and side effects of all drugs, not after the administration of the drugs, but in advance based on the information of genetic polymorphism. Furthermore, the automation of such a method as taught by Rienhoff et al. would have been obvious because it would

increase efficiency of testing and data management. Therefore, to use the computer program product taught by Rienhoff et al. to automate the method taught by ICHIKAWA, one of ordinary skill in the art would have recognized that applying the known technique would have yielded predictable results and resulted in an improved method.

Ichikawa and Rienhoff et al. suggest, but do not explicitly teach displaying a first user interface to a clinician, the user interface configured to display and receive clinical agent information including at least one identifier of a clinical agent as in step a) and displaying a second user interface to the clinician configured to display the output as in step g).

Fey et al. teach at paragraphs [0022] [0048] and [0055] an application of health data management which involves a graphical user interface written for web browser applications wherein the user has a unique identification and may enter information through the GUI. Fey et al. at paragraph [0012] teach keeping secure health records, which are accessible by authorized health persons. Fey et al. further teach that custom reports are generated at the time tests are performed that explains the results. Fey et al. teach at paragraph [0022] wherein results are prepared for the individual and physician. Fey et al. teach at paragraph [0047] wherein the health data may be used by doctors. In addition, Fey et al. at paragraphs [0053] – [0059] and [0063] – [0075] teach a system comprising a means, i.e. a displaying component and computer storage media configured for displaying a graphical user interface. With further regards to claim 23, Fey et al. teach at paragraph [0031] storing the genetic test results.

Fey et al. does not explicitly teach a GUI that is configured to solicit input from a clinician to ascertain an identifier of a clinical agent as in step b) or whether to authorize performing a genetic test on a patient. In fact, Fey et al. teach, i.e. paragraph [0057] that the invention is directed to enabling a client/consumer to order genetic testing without doctor's approval. Furthermore, Fey et al. teach that a client can use the taught invention to determine genetic risk towards disease or conditions or discover genetic predispositions.

It is noted that the functionality of Fey's system, not the method steps, is what is relied upon in the instant rejection. The invention taught by Fey et al. has the functionality of using a graphical user interface to solicit input, albeit from a client, to ascertain whether to perform a genetic test, displays identification of the genetic test to be performed, receives approval or authorization from the client to carry out the genetic test, ensures identification of the person, and is configured to receive result value of the genetic test for the person.

Fiedotin et al. at the abstract, Fig. 3a-4d, col. 6, lines 45-54, col. 12, lines 64-67 and col. 13, lines 1-6 teach various graphical user interfaces for displaying clinical agent information, warnings about contraindications or adverse reactions and other information.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used a system for displaying information and receiving clinician input as taught as taught by Fey et al. and Fiedotin et al. for use in the invention taught by Ichikawa and REINHOFF. This is because the use of graphical user interfaces for

displaying information or receiving clinician input as taught by Fey et al. and Fiedotin et al. for use in known methods as taught by Ichikawa and REINHOFF is seen as the automation of known methods. Automation of known methods is an obvious step or improvement because the automation, i.e. use of computers, to perform otherwise known methods is not an unobvious variation from the teachings of prior art wherein automation was not performed. In other words, broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art (see In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958)). Furthermore, one of ordinary skill in the art could have applied the known improvements, i.e. the use of graphical user interfaces in known methods and the results would have been predictable to one of ordinary skill in the art. Moreover, a skilled artisan would find that the differences between the claimed invention and the prior art were encompassed in known variations or in a principal known in the prior art.

The combination of Ichikawa, REINHOFF, Fey et al., and Fiedotin et al. do not explicitly teach an agent-gene association table.

Hogan at Fig. 4 teaches an agent-gene association table. In addition, Hogan at the abstract teaches screening patients for markers indicative of responses to drugs and treatments to tailor a subject's medical or surgical treatment to reflect genetic information.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used an agent-gene association table such as that taught by

Hogan for use in the method for displaying information on one or more user interfaces regarding the likelihood a person has a gene variant indicative of an atypical event as taught by the combination of Ichikawa, REINHOFF, Fey et al., and Fiedotin et al. This is because Ichikawa also teach the benefit of having this information in order to tailor treatments to a patient's genomic profile. Therefore, the known technique of determining using agent-gene association information along with a patient's genomic profile was recognized as part of the ordinary capabilities of one skilled in the art. One of ordinary skill in the art would have been capable of applying this known technique to the taught method and the results would have been predictable to one of ordinary skill in the art.

ICHIKAWA also teaches at page 523, second column, paragraphs 1 and 2, wherein the hereditary information includes ethnicities as in claims 3, 10, and 17.

Rienhoff et al. at paragraphs [0006]-[0007] teach the use of comprehensive medical databases for storing hereditary information. Furthermore, Rienhoff et al. at paragraph [0011]-[0012] teach determining, storing, and comparing polymorphic genomic profiles of individuals in databases wherein these databases are used to assist in performing clinical trials and drug administration (see paragraph [0014]), which reads on a broad interpretation of a comprehensive healthcare system as in claims 5, 12, and 19.

Reinhoff et al. at paragraph [0010] teach a computer program that allows identification of a susceptibility locus in individuals using genetic screening methods to assess individuals' risk of certain diseases. Reinhoff et al. at paragraph [0011] teach

determining a statistically significant difference between the polymorphic profiles for each individual of the population and separating the population into a first subpopulation and a second subpopulation based up the profiles. Reinhoff et al. teach at paragraph [0014] wherein databases may be updated and expanded. Moreover, Reinhoff et al. at paragraph [0027] teach how an individual's polymorphic profile can be ordered and stored, which reads on claims 6, 13, and 20 and limitations of claims 7,14, and 21.

Fiedotin et al. at the abstract, Fig. 3a-4d, col. 6, lines 45-54, col. 12, lines 64-67 and col. 13, lines 1-6 teach various graphical user interfaces for displaying clinical agent information, warnings about contraindications or adverse reactions and other information, such as other alternative drugs in the same class that may be used, which reads on the other limitations of claims 7, 14, and 21.

REINHOFF teach at paragraph [0076] claim 22.

Response to Arguments

Applicant's arguments filed 6/21/2010 have been considered, but are not found persuasive.

Applicant at pages 15-19 of the responses summarize their claim amendments and specifically to independent claims 1, 8, and 15.

Applicant at page 19 argues that the Ichikawa reference fails to teach or suggest receiving inputs from the clinician including an identifier of a clinical agent and a dosage of the clinical agent to be administered to the patient where the clinician selects the clinical agent from a listing of clinical agents on a graphical user interface and where the

clinician selects a specific dosage of the clinical agent from a range of dosages recommended for the clinical agent associated with the selected entry.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Furthermore, Ichikawa teaches the relatedness between drug dosages, patient responses, and patient genomic profiles, such as patients with TPMT deficiency accumulate higher levels of thioguanine if they receive standard doses. As such Ichikawa teaches that “it is quite important to know in advance whether a patient who will be treated with thiopurine derivatives, has genetic polymorphism at TPMT site.” Ichikawa further teaches performing a test to obtain the genomic profile information. In addition, Ichikawa states that “as shown in this paper, we may be able to know beforehand from the information of genetic polymorphism, whether a patient will respond or show adverse effects, and may know further the proper dosage for each patient." Thus Ichikawa teaches the motivation to see if there is a relationship between genomic profiles, drug treatments, and responses and to look further into determining if known genomic profiles exist for a patient before a treatment or drug is administered. Ichikawa states "it would become possible to anticipate the effectiveness and side effects of all drugs, not after administration of the drugs, but in advance based on the information of genetic polymorphism as shown in the drug metabolism of azathioprine.”

Hogan as described above teaches a table of agent-gene association information.

Applicant further argues that Reinhoff does not teach said limitations.

Applicant's arguments are not found persuasive because Reinhoff was used to show the obviousness of computerizing and/or automating aspects when combined with the Ichikawa reference.

Applicant further argues at page 21 that the Fey reference fails to cure the deficiencies of the Ichikawa and Reinhoff references, such as receiving from a graphical user interface a clinician's inputs including at least one identifier of a clinical agent and a dosage of the clinical agent, where receiving includes receiving a selection of an entry in a listing of clinical agents on the first user interface and a selection of the dosage from a range of dosages recommended for the clinical agent associated with the selected entry.

Applicant's arguments are not found persuasive as Ichikawa describes at least one identifier of a clinical agent and a dosage of the clinical agent with regards to a treatment based on a patient's genomic profile. The combination of the Fey et al, Reinhoff, Fiedotin, and Hogan, make obvious the computerization and use in a clinical setting for a clinician to supply input and receive information.

Applicant further argues that Fey is silent on accesing an agent-gene association table.

Applicant's arguments are not found persuasive because Hogan teaches using and providing an agent-gene association table.

Applicant at page 22 makes the same argument with regards to the Fiedotin reference.

Applicant's arguments are not found persuasive as already described above.

Applicant at page 23 makes the same argument with regards to the Harris reference.

Applicant's arguments are not found persuasive as already described above.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/ Jason Sims /

/Marjorie Moran/

Supervisory Patent Examiner, Art Unit 1631